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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,229	12/20/2001	George Jackowski	2132.113	3487

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EXAMINER	
BALLARD, KIMBERLY A	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
09/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/032,229	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-12 and 15-17* is/are pending in the application.

4a) Of the above claim(s) *15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 16, 2007 has been entered.

Response to Amendment

2. Claim 15 has been amended as requested in the amendment filed on July 16, 2007. Following the amendment, claims 5-12 and 15-17 are pending in the instant application.

3. Claims 5-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 27, 2005.

4. Claims **15-17** are under examination in the instant office action.

Withdrawn Claim Rejections

5. The rejection of claims 15-17 under 35 USC § 112, first paragraph, as set forth in the previous Office action, is withdrawn in view of Applicants' amendments to the claims.

Maintained Claim Rejections

Claim Rejections - 35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. The rejection of claims 16-17 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained for reasons of record.

Claim 15 recites the phrase "a thrombospondin polypeptide weighing about 180 kDa", which is indefinite because the claim does not specify the manner in which the molecular weight was determined (native PAGE, denaturing SDS-PAGE, predicted from sequence, etc.) It is well known in molecular biology that the value of the molecular weight for a given protein depends entirely upon the manner in which it is determined. Therefore, the recitation of the molecular weight in the claim is not meaningful, as the metes and bounds of the claim cannot be ascertained. Claims 16-17 are similarly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for being dependent from indefinite rejected claim 15.

It is noted that Applicants did not specifically address this rejection in the response filed July 16, 2007. The rejection therefore is maintained for reasons of record.

Claim Rejections - 35 USC § 102

8. The rejection of claims 15-17 under 35 USC § 102(e), as set forth in previous Office actions is maintained for reasons of record. Claims 15-17 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,605,592 to Ni et al. or in the alternative US PGPub 20020068319 by Ni et al., as evidenced by Asakura et al. (*J. Neuroimmunol.* 1996; **65**:11-19). The Ni et al. references are cumulative and are therefore cited together with identical reasoning therefore.

In the response filed July 16, 2007, Applicants argue that the THRAP protein taught by Ni et al. is simply not equivalent to thrombospondin, and that the claimed molecular weight of about 180 kDa (as established by gel electrophoresis) is different from the "about 190" of the Ni et al. reference. Applicants assert that any changes to the changes to the sequence of a peptide may have a substantial effect on binding, and therefore the ability of a diagnostic assay to function with the degree and specificity required. Further, Applicants argue that not every limitation of the claim has been met, and therefore the use of "inherency" allegations as a means of rationalizing maintenance of an anticipatory reference under 35 USC 102 is insufficient in this case. Applicants appear to argue that the Ni et al. disclosure may not be enabled as an anticipatory reference under 35 USC 102 because of the unpredictability in the art and

the degree of experimentation required (i.e., the Wands factors) to ascertain the facts as alleged by the Examiner. Accordingly, Applicants submit that the THRAP protein taught by Ni et al. which shares regions of identity with a "thrombospondin-like protein" is "a far cry from a teaching that THRAP is equivalent to the thrombospondin peptide of the instant invention," and it cannot be predicted that the THRAP protein is anticipatory of the claimed "about 180 kDa" peptide of the instant claims.

Applicants' arguments have been fully considered, but they are not deemed to be persuasive. Ni et al. teach immunoassay methods for the detection of THRAP polypeptide and/or fragments thereof in a biological sample, such as from blood, for the diagnosis of Alzheimer's disease in a human patient (see column 91, lines 27-37). As noted previously, the THRAP protein taught by Ni et al. exhibits 13 thrombospondin-1 (TSP-1)-like domains (see Figure 4) and shares substantial homology with thrombospondin-like protein (see Figure 5). The THRAP disclosed by Ni et al. with its predicted molecular weight of about 190 kDa thus bears a striking similarity, both in terms of amino acid sequence and predicted molecular weight, to the thrombospondin peptide of about 180 kDa instantly recited. Besides, as noted previously, the recitation of the molecular weight in the claims is not meaningful because it is well known in molecular biology that the value of the molecular weight for a given protein depends entirely upon the manner in which it is determined, and thus Ni fully anticipates this limitation.

Moreover, the crux of the claimed diagnostic method rests upon the use of "at least one antibody" to specifically bind to and detect a thrombospondin polypeptide

weighing about 180 kDa. There is no teaching in the art, nor any factual evidence brought forth on record, to indicate that the antibodies of the diagnostic immunoassays taught by Ni would not be capable of binding to and detecting the instantly claimed thrombospondin polypeptide. For example, Ni identifies highly antigenic regions of the THRAP protein. Because of the significant overlap in amino acid sequences and antigenic epitopes between the THRAP protein and the thrombospondin polypeptide, the skilled artisan would reasonably expect that an antibody directed against the THRAP protein would also be able to recognize and bind to a thrombospondin polypeptide. Thus, it would also be expected that the antibodies disclosed by Ni for detection of THRAP protein and diagnosis of Alzheimer's disease would be capable of detecting thrombospondin and diagnosing Alzheimer's dementia as instantly claimed. As noted previously, the art recognizes that antibodies, even monoclonal antibodies, are notoriously promiscuous in terms of their capacity to bind similar epitopes on different proteins. See, for example, Asakura et al., which evidence that a monoclonal antibody (designated SCH94.03) was capable of specifically recognizing five different proteins: rat kinesin light chain, mouse thrombospondin-1, mouse oncofetal antigen, RNA polymerase beta subunit, and nuclear phosphoprotein (see abstract). It is thus Applicants' burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicants' claims.

Moreover, with respect to Applicants' argument that the Ni et al. reference may not be enabling for the detection of a thrombospondin polypeptide as instantly claimed, MPEP § 2121, states that:

> When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

As the goal of the claimed methods (i.e., diagnosis of Alzheimer's disease), the population tested (i.e., patients suspected of having Alzheimer's), the technique used (i.e., immunoassay using a specific antibody), the expected binding specificity of the antibody, and the similarly in sequence and antigenic homology between the broadly claimed antigen (i.e., *a* thrombospondin polypeptide weighing *about* 180 kDa) and the THRAP protein of Ni are the same in both the current invention and the Ni reference, the ability to detect such a thrombospondin polypeptide in a patient sample would inherently be expected for diagnosis of Alzheimer's dementia. Accordingly, the rejection of instant claims 15-17 as being anticipated by the teachings of Ni et al. is maintained.

Conclusion

9. No claims are allowed.

10. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE**

FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on Monday-Friday 9AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
September 1, 2007

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646